## REMARKS

*Rejection Under 35 U.S.C. § 103*

Claims 1, 3-5 and 9-16 stand rejected under 35 U.S.C. 103 over Reynolds US 3,808,332 in view of Lindenbaum (WO 93/04691) and further in view of Jacobs et al.(US 2005/003491). Reconsideration of this rejection is respectfully requested.

Reynolds discloses a pharmaceutical composition comprising a carrier and the reaction product of tertiary phosphine with thyroxine and 3, 5, 3 prime-L-triiodothyronine. The Office Action admits, at page 2 that Reynolds fails to teach gelatin in the combination.

The Examiner relies upon Lindenbaum for its suggestion regarding the use of pharmaceutical preparations containing levothyroxine or triiodothyronine and gelatin.

However, Lindenbaum is directed to topical applications (i.e., wound treatment formulations," where "wound" refers to wounds of the skin). Lidenbaum does not deal with preparations in tablet or solid form. Pharmaceutical compositions of Lidenbaum involve a "delivery polymer," see page 6, paragraph 3 and page 16, the second full paragraph bridging to pages 17. Such delivery polymers include a hydrogel such as HEMA (hydroxyethyl-methacrylate) or NVP (N-vinylpyrrolidone), polyethylene glycol (PEG), gelatin, agarose, methylcellulose and related hydrophilic cellulose polymers or collagen. The delivery polymer is stated to exhibit the added benefit of slowing formation of a scab on the wound. Additionally, as can be seen on page 18, example 1, a lyophilized powder is reconstituted as a gel *using* gelatin in order to apply topically. Thus, once the gelatin has been added the pharmaceutical preparation it is in the form of a gel and not a powder. Gels, creams, etc. are known in the art as "semi-solids", not solid formulations.

On page 3 of the Office Action the Examiner states: "The present claims are entirely drawn to compositions comprising levothyroxine and optionally liothyronine and gelatin. Accordingly, intended use is not a consideration and does not impart patentability to a composition that is obvious from prior art teaching." This is irrelevant to the forgoing arguments because the discussed aspects are claim features.

It is thus respectfully submitted that one of ordinary skill in the art looking to produce

*tablets or solid* form preparations suitable for oral administration would not look to the topical formulation disclosure of Lindenbaum for any suggestion of the use of gelatin. Neither Reynolds nor Lindenbaum suggest formulations using gelatin as a binder in a *tablet or solid* formulation.

Jacobs et al.(US 2005/003491) deals with secreted proteins and polynucleotides encoding them. The Examiner relies upon Jacobs et al. for teaching gelatin in solid pharmaceutical formulations comprising proteins. See page 174, paragraph 4072.

Jacobs is silent regarding thryroxin or levo-thyroxin. Beginning on page 174 Jacobs discloses numerous administration routes and dosage forms. For example, the compositions of Jacobs may be administered topically, systematically, or locally as an implant or device. They may be administered by intravenous, cutaneous or subcutaneous injection. The compositions may be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the pharmaceutical composition may additionally contain a solid carrier such as a gelatin or an adjuvant. Thus, Jacobs broadly discloses numerous administration routes and dosage forms, none of which deal with thryroxin or levo-thyroxin. A skilled worker dealing with the problem of stabilization of levo-thyroxin would simply not look towards a broad generic disclosure that deals with numerous administration forms of entirely different proteins for guidance.

In any event, as established on record, even if there were a prima fascia case of obviousness, the declaration filed on 13 February 2008 overcomes it by establishing unexpected properties. However, on page 4 of the Office Action the Examiner states:

> "In Formulation B it is unclear whether or not hydroxypropyl methylcellulose imparts a de-stabilizing effect."

Hydroxypropyl methylcellulose is a well-known conventional binder, which is very common in the manufacture of pharmaceutical tablets. This is established by the cited references even. See, Jacobs at paragraph 4080 and Lindenbaum page 17, line 1-7. Why would such a component be a common ingredient if it were expected to impart instability? The Examiner expresses doubt but does not provide any evidence, facts or reasoning sufficient to justify her allegation that hydroxypropyl methylcellulose might impart a de-stabilizing effect. All evidence is to the contrary. The Office Action simply does

not provide sufficient basis in support of a *reasonable* doubt on this issue.

It is clearly shown by the data provided in the declarations of Dr. Schaffler and Dr. Lindenblatt that an increase of gelatin unexpectedly increases the stability of the formulation. The improvement in stability increases with the amount of gelatin. This alone clearly proves the stabilizing effect of gelatin, and is enough to establish non-obviousness. Even if HPMC were a destabilizer (not established) this would not affect the unexpectedness of including gelatin to enhance stability.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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